



## SEQUENCE LISTING

<110> Bougueleret, Lydie  
Bairoch, Amos  
Niknejad, Anne

<120> Engineered Human Kunitz-Type Protease  
Inhibitor

<130> 54720-8015.US00

<140> US 10/807,204  
<141> 2004-03-22

<150> PCT/EP03/01629  
<151> 2003-02-18

<150> US 60/358,683  
<151> 2002-02-21

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Ile Pro His Trp Trp Tyr Asn Lys Lys Thr Lys Ile Cys Ser Glu Phe
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Pro Cys Pro Lys Ile Lys Val Glu Cys

35

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tatggttaga	atatcttact	tttgacagata	ttacaagtca	tctgacctg	taaacatata	9131
gctagaagca	ctcccagaat	cttaaaaagg	gctcgctcga	gcgaggacc	tgaggcttgg	9191
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tgtagtaaa	aagacagttc	catagtattg	tgcaaaaact	ccaaaattga	aaatagctgg	9311
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ggctaagcta	gaataagtgc	aagtcctact	tgatcctctt	atgtagcttg	tttgggggca	9611
gtgggaaact	gccatgtaag	atgtccaact	actctgagag	aggcccatgc	tagagagacc	9671
catgtgggtg	ctgtgatcag	caggccca	taagctctga	ctgatagcca	gcatcaattt	9731
cagccatgca	aatgagatgc	ccaacccaat	agagccttca	gatggctgca	gccccagcag	9791
acatctgact	gcaaccatgg	gaaagaccct	ataaaaaga	caccaagcag	attgcttccc	9851
agatggctga	cccacaatat	aaaatggttg	ctttaaagt	ctaagttttc	agaaaattta	9911
ttcacagaat	aggtgatcaa	agatggaac	gggctaggag	cagtggctca	cagctgta	9971
cccaggcact	ttgggagtcc	aaggcaggca	gataaactga	agtcagaagt	tcaagaccag	10031
cctggccaaa	acggcaaa	cctgtctcta	ctaaaaatac	aaaaattagc	cagacatagt	10091
ggcgggcacc	tgtaatacca	cctactcggg	aggctggggc	aggagaatct	cttcagccc	10151
ggaggcgag	gttgcatgga	gctgagattg	cgccactgca	ctccagagcg	agatttggtc	10211
tcaaaaaaaa	aaaaagaa	aaaaaaaaga	tgaaaaggga	gtagaaggaa	ggataggag	10271
agagaaagaa	gaaagagaca	cccataggac	tgggcaagat	aagaggatgc	caggcttgag	10331
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caaataagtt	tgttgtttta	tataacttgg	atcaaggggc	tctaaagagg	ctggaattca	10451
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gattgtagaa	aactctaaag	gcactgcaaa	aaaagggttag	aattaataaa	caaattttatt	10571
aaagttacag	gatacaaaat	caacatacaa	aaatcaatag	caactttata	caccaagaac	10631
aatctcattt	ccatcagcgg	caacaacaac	aaaacactca	gtaatttaact	caaccaaaga	10691
agtgaaaaac	ttatgcattg	acaattataa	aacatcgatg	aaggaaattt	aaaagacaca	10751
aataaatgaa	aagacatcca	tgctcataga	ttagaagaat	caatgttgtc	aaaatgtcca	10811

cactacccaa agcaatctac agagcacatg caatttctgc caaaatgccca atggcatttt 10871  
 ttacagaaac ataaaaagca atgctaaaat tcatatggaa ccacaaaaga ccccaaattg 10931  
 ccaaaggaat ttgtaaaaag aacagagctg taagcaccac atttcctgat gtcaaattac 10991  
 attgcaaagc tagagtaatc aaaagagtgt ggtactggca taaaaacaga aaagcagaca 11051  
 tacaggccaa tggaacagaa tagagaagcc agaactaagc ccaccattt atggtcaatt 11111  
 gatctttgac gagggtgtca aaaacacaca ataggcaaca gaagatctct ttaacaaatg 11171  
 gtgctgggaa aactagatat tcacatgcaa 11201

<210> 4  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 4  
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 1 5 10 15  
 Gly Asp Ile Gln Glu Pro Gly His Ala Glu Gly Ile Leu Gly  
 20 25 30

<210> 5  
 <211> 43  
 <212> PRT  
 <213> Homo sapiens

<400> 5  
 Pro Cys Pro Lys Ile Lys Val Glu Cys Glu Val Glu Glu Ile Asp Gln  
 1 5 10 15  
 Cys Thr Lys Pro Arg Asp Cys Pro Glu Asn Met Lys Cys Cys Pro Phe  
 20 25 30  
 Ser Cys Gly Lys Lys Cys Leu Asp Phe Arg Lys  
 35 40

<210> 6  
 <211> 24  
 <212> PRT  
 <213> Homo sapiens

<400> 6  
 Asp Ile Cys Ser Met Pro Gln Glu Ala Gly Pro Cys Leu Ala Ser Ile  
 1 5 10 15  
 Pro His Trp Trp Tyr Asn Lys Lys  
 20

<210> 7  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 7  
 Thr Lys Ile Cys Ser Glu Phe Ile Tyr Gly Gly Ser Gln Gly Asn Asn  
 1 5 10 15  
 Asn Asn Phe Gln Thr Glu Ala Ile Cys Leu Val Thr Cys Lys Lys Tyr  
 20 25 30  
 His

<210> 8



<211> 1339  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(1339)  
 <223> reconstructed cDNA from SEQ ID NO:3

<221> CDS  
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<221> CDS  
 <222> (296)...(394)

<221> misc\_feature  
 <222> (394)...(396)  
 <223> potential stop codon

<221> 3'UTR  
 <222> (397)...(1339)  
 <223> partial

<221> polyA\_signal  
 <222> (1334)...(1339)

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 Met Gly Leu Ser Gly Leu Leu Pro Ile Leu Val Pro Phe Ile Leu Leu  
 1 5 10 15  
 ggg gac atc cag gaa cct ggg cac gct gaa ggc atc ctt ggc aag ccg 96  
 Gly Asp Ile Gln Glu Pro Gly His Ala Glu Gly Ile Leu Gly Lys Pro  
 20 25 30  
 tgt ccc aaa atc aaa gtg gaa tgc gaa gtg gaa gaa ata gac cag tgt 144  
 Cys Pro Lys Ile Lys Val Glu Cys Glu Val Glu Glu Ile Asp Gln Cys  
 35 40 45  
 acc aaa ccc aga gat tgc cca gaa aac atg aag tgt tgc ccg ttc agc 192  
 Thr Lys Pro Arg Asp Cys Pro Glu Asn Met Lys Cys Cys Pro Phe Ser  
 50 55 60  
 cgt gga aag aaa tgt tta gac ttc aga aag gat ata tgc agt atg cca 240  
 Arg Gly Lys Lys Cys Leu Asp Phe Arg Lys Asp Ile Cys Ser Met Pro  
 65 70 75 80  
 cag gag gct ggc ccc tgc ctg gcc tcc ata cca cac tgg tgg tac aat 288  
 Gln Glu Ala Gly Pro Cys Leu Ala Ser Ile Pro His Trp Trp Tyr Asn  
 85 90 95  
 aaa aaa a act aag atc tgc tcc gaa ttc atc tat ggc ggt agc cag ggg 337  
 Lys Lys Thr Lys Ile Cys Ser Glu Phe Ile Tyr Gly Gly Ser Gln Gly  
 100 105 110  
 aac aat aac aac ttc caa act gaa gct atc tgt ctg gtc acc tgc aaa 385  
 Asn Asn Asn Asn Phe Gln Thr Glu Ala Ile Cys Leu Val Thr Cys Lys

115

120

125

aaa tac cat aagtcaccaga ggtcccggtc tcctgtgctc accaaggcca  
 Lys Tyr His  
 130

434

cactgggagg tctgggtggt ggctgggtcta ttccaagacc tgggtggcgc tggggatgac 494  
 aaaaccagct ccaatgcaga agtataagta gaaggatatt ttgggaaaga ggggtgggaag 554  
 ggagggatta gtcaaaggga tattggcaag tatgagggtga gtagtgggtg tagagagaaa 614  
 acagaagtgg tggagtatcc cagaccaggt cagacggaag cccggtaaac ccagcccagc 674  
 cctgggcacc attcatcagc caatcattat agtcctttac ttctcactaa accttgttgc 734  
 tacttctctt cctttgaaag gttatttcta accagggcaa ccacatactt tattggccaa 794  
 accaaatcac ttttgaaagt gtctcaaggt gaggtgccat taattattac actgagacaa 854  
 caggcataaa ctgggactct actggacaag tcagaactca tgatcattct aggagccccc 914  
 aaactcacct tcattccatt cctgccc aaa gatgtaaaaa tgatcccacc tcctttttcc 974  
 cattaggtgc aagatttgggt tcctaattgtg gtcagggtcc aagcatctca ccctttattc 1034  
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 ccacgggcca aaccttggct gttccagaaa ctgaacccca ggaattgctt acacactttc 1214  
 ttccagcgta gcatctcttc aaacacaatg ctcttcccct tgaccacttc tcagtatgaa 1274  
 actctatgtc ttcaactttc agacccccca tttatttcta tgaaggcttc agttgcctta 1334  
 ataaa 1339

&lt;210&gt; 9

&lt;211&gt; 98

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 9

Met Gly Leu Ser Gly Leu Leu Pro Ile Leu Val Pro Phe Ile Leu Leu  
 1 5 10 15  
 Gly Asp Ile Gln Glu Pro Gly His Ala Glu Gly Ile Leu Gly Lys Pro  
 20 25 30  
 Cys Pro Lys Ile Lys Val Glu Cys Glu Val Glu Glu Ile Asp Gln Cys  
 35 40 45  
 Thr Lys Pro Arg Asp Cys Pro Glu Asn Met Lys Cys Cys Pro Phe Ser  
 50 55 60  
 Arg Gly Lys Lys Cys Leu Asp Phe Arg Lys Asp Ile Cys Ser Met Pro  
 65 70 75 80  
 Gln Glu Ala Gly Pro Cys Leu Ala Ser Ile Pro His Trp Trp Tyr Asn  
 85 90 95  
 Lys Lys

&lt;210&gt; 10

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 10

Thr Lys Ile Cys Ser Glu Phe Ile Tyr Gly Gly Ser Gln Gly Asn Asn  
 1 5 10 15  
 Asn Asn Phe Gln Thr Glu Ala Ile Cys Leu Val Thr Cys Lys Lys Tyr  
 20 25 30  
 His

<210> 11  
 <211> 396  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(396)  
 <223> reconstructed cDNA for SEQ ID NO:1

<221> CDS  
 <222> (1)...(396)

<400> 11  
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 Met Gly Leu Ser Gly Leu Leu Pro Ile Leu Val Pro Phe Ile Leu Leu  
 1 5 10 15  
 ggg gac atc cag gaa cct ggg cac gct gaa ggc atc ctt ggc aag ccg 96  
 Gly Asp Ile Gln Glu Pro Gly His Ala Glu Gly Ile Leu Gly Lys Pro  
 20 25 30  
 tgt ccc aaa atc aaa gtg gaa tgc gaa gtg gaa gaa ata gac cag tgt 144  
 Cys Pro Lys Ile Lys Val Glu Cys Glu Val Glu Glu Ile Asp Gln Cys  
 35 40 45  
 acc aaa ccc aga gat tgc cca gaa aac atg aag tgt tgc ccg ttc agc 192  
 Thr Lys Pro Arg Asp Cys Pro Glu Asn Met Lys Cys Cys Pro Phe Ser  
 50 55 60  
 cgt gga aag aaa tgt tta gac ttc aga aag gat ata tgc agt atg cca 240  
 Arg Gly Lys Lys Cys Leu Asp Phe Arg Lys Asp Ile Cys Ser Met Pro  
 65 70 75 80  
 cag gag gct ggc ccc tgc ctg gcc tcc ata cca cac tgg tgg tac aat 288  
 Gln Glu Ala Gly Pro Cys Leu Ala Ser Ile Pro His Trp Trp Tyr Asn  
 85 90 95  
 aaa aaa act aag atc tgc tcc gaa ttc atc tat ggc ggt tgc cag ggg 336  
 Lys Lys Thr Lys Ile Cys Ser Glu Phe Ile Tyr Gly Gly Cys Gln Gly  
 100 105 110  
 aac aat aac aac ttc caa act gaa gct atc tgt ctg gtc acc tgc aaa 384  
 Asn Asn Asn Asn Phe Gln Thr Glu Ala Ile Cys Leu Val Thr Cys Lys  
 115 120 125  
 aaa tac cat taa 396  
 Lys Tyr His \*  
 130

<210> 12  
 <211> 131  
 <212> PRT  
 <213> Homo sapiens

<400> 12

Met	Gly	Leu	Ser	Gly	Leu	Leu	Pro	Ile	Leu	Val	Pro	Phe	Ile	Leu	Leu
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Gly	Asp	Ile	Gln	Glu	Pro	Gly	His	Ala	Glu	Gly	Ile	Leu	Gly	Lys	Pro
			20					25					30		
Cys	Pro	Lys	Ile	Lys	Val	Glu	Cys	Glu	Val	Glu	Glu	Ile	Asp	Gln	Cys
		35					40					45			
Thr	Lys	Pro	Arg	Asp	Cys	Pro	Glu	Asn	Met	Lys	Cys	Cys	Pro	Phe	Ser
	50					55					60				
Cys	Gly	Lys	Lys	Cys	Leu	Asp	Phe	Arg	Lys	Asp	Ile	Cys	Ser	Met	Pro
65					70					75					80
Gln	Glu	Ala	Gly	Pro	Cys	Leu	Ala	Ser	Ile	Pro	His	Trp	Trp	Tyr	Asn
				85					90					95	
Lys	Lys	Thr	Lys	Ile	Cys	Ser	Glu	Phe	Ile	Tyr	Gly	Gly	Cys	Gln	Gly
			100					105					110		
Asn	Asn	Asn	Asn	Phe	Gln	Thr	Glu	Ala	Ile	Cys	Leu	Val	Thr	Cys	Lys
		115					120					125			
Lys	Tyr	His													
	130														

<210> 13  
 <211> 133  
 <212> PRT  
 <213> Homo sapiens

Met	Gly	Ser	Ser	Gly	Leu	Leu	Ser	Leu	Leu	Val	Leu	Phe	Val	Leu	Leu
1				5					10					15	
Ala	Asn	Val	Gln	Gly	Pro	Gly	Leu	Thr	Asp	Trp	Leu	Phe	Pro	Arg	Arg
			20					25					30		
Cys	Pro	Lys	Ile	Arg	Glu	Glu	Cys	Glu	Phe	Gln	Glu	Arg	Asp	Val	Cys
		35					40					45			
Thr	Lys	Asp	Arg	Gln	Cys	Gln	Asp	Asn	Lys	Lys	Cys	Cys	Val	Phe	Ser
	50					55					60				
Cys	Gly	Lys	Lys	Cys	Leu	Asp	Leu	Lys	Gln	Asp	Val	Cys	Glu	Met	Pro
65					70					75					80
Lys	Glu	Thr	Gly	Pro	Cys	Leu	Ala	Tyr	Phe	Leu	His	Trp	Trp	Tyr	Asp
				85					90					95	
Lys	Lys	Asp	Asn	Thr	Cys	Ser	Met	Phe	Val	Tyr	Gly	Gly	Cys	Gln	Gly
			100					105					110		
Asn	Asn	Asn	Asn	Phe	Gln	Ser	Lys	Ala	Asn	Cys	Leu	Asn	Thr	Cys	Lys
		115					120					125			
Asn	Lys	Arg	Phe	Pro											
	130														

<210> 14  
 <211> 134  
 <212> PRT  
 <213> Mus musculus

Met	Lys	Leu	Ser	Gly	Phe	Val	Ser	Ile	Leu	Val	Leu	Phe	Gly	Leu	Leu
1				5					10					15	
Ala	Arg	Val	Gln	Gly	Pro	Ser	Leu	Ala	Asp	Leu	Leu	Phe	Pro	Arg	Arg
			20					25					30		
Cys	Pro	Arg	Phe	Arg	Glu	Glu	Cys	Glu	His	Gln	Glu	Arg	Asp	Leu	Cys
		35					40					45			
Thr	Arg	Asp	Arg	Asp	Cys	Pro	Lys	Lys	Glu	Lys	Cys	Cys	Val	Phe	Asn

50		55		60
Cys Gly Lys Lys Cys	Leu Asn Pro Gln Gln Asp	Ile Cys Ser Leu Pro		
65	70	75	80	
Lys Asp Ser Gly Tyr	Cys Met Ala Tyr Phe Arg Arg	Trp Trp Phe Asn		
	85	90	95	
Lys Glu Asn Ser Thr	Cys Gln Val Phe Ile Tyr Gly Gly	Cys Gln Gly		
	100	105	110	
Asn Asn Asn Asn Phe	Gln Ser Gln Ser Ile Cys Gln	Asn Ala Cys Glu		
	115	120	125	
Lys Lys Ser Ser Leu Thr				
130				

<210> 15  
 <211> 131  
 <212> PRT  
 <213> Homo sapiens

<400> 15
Met Gly Leu Ser Gly Leu Leu Pro Ile Leu Val Pro Phe Ile Leu Leu
1 5 10 15
Gly Asp Ile Gln Glu Pro Gly His Ala Glu Gly Ile Leu Gly Lys Pro
20 25 30
Cys Pro Lys Ile Lys Val Glu Cys Glu Val Glu Glu Ile Asp Gln Cys
35 40 45
Thr Lys Pro Arg Asp Cys Pro Glu Asn Met Lys Cys Cys Pro Phe Ser
50 55 60
Arg Gly Lys Lys Cys Leu Asp Phe Arg Lys Asp Ile Cys Ser Met Pro
65 70 75 80
Gln Glu Ala Gly Pro Cys Leu Ala Ser Ile Pro His Trp Trp Tyr Asn
85 90 95
Lys Lys Thr Lys Ile Cys Ser Glu Phe Ile Tyr Gly Gly Ser Gln Gly
100 105 110
Asn Asn Asn Asn Phe Gln Thr Glu Ala Ile Cys Leu Val Thr Cys Lys
115 120 125
Lys Tyr His
130

<210> 16  
 <211> 136  
 <212> PRT  
 <213> Mus musculus

<400> 16
Met Arg Leu Trp Gly Leu Leu Pro Phe Leu Val Pro Phe Ile Leu Leu
1 5 10 15
Trp Ser Ile Gln Glu Pro Glu Leu Ala Glu Gly Phe Phe Ile Arg Thr
20 25 30
Cys Pro Arg Val Arg Val Lys Cys Glu Val Glu Glu Arg Asn Glu Cys
35 40 45
Thr Arg His Arg Gln Cys Pro Asn Lys Lys Arg Cys Cys Leu Phe Ser
50 55 60
Cys Gly Lys Lys Cys Met Asp Leu Arg Gln Asp Val Cys Ser Leu Pro
65 70 75 80
Gln Asp Pro Gly Pro Cys Leu Ala Tyr Leu Pro Arg Trp Trp Tyr Asn
85 90 95
Gln Glu Thr Asp Leu Cys Thr Glu Phe Ile Tyr Gly Gly Cys Gln Gly
100 105 110

Asn	Pro	Asn	Asn	Phe	Pro	Ser	Glu	Gly	Ile	Cys	Thr	Val	Val	Cys	Lys
		115					120					125			
Lys	Lys	Gln	Met	Ser	Ser	Trp	Ile								
	130					135									